



NicOx announces favorable blood pressure data for naproxcinod in a large ABPM study

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NicOx S.A. (Euronext Paris: COX) today announced positive top-line results from a 118 patient Ambulatory Blood Pressure Monitoring (ABPM) trial (the 111 study), which compared the 24-hour blood pressure profile of escalating doses of naproxcinod and naproxen in osteoarthritis (OA) patients with controlled hypertension. The primary ABPM parameter was the mean 24-hour ambulatory systolic blood pressure (SBP) measured by ABPM over the whole study period and naproxcinod showed a statistically significant decrease in SBP of 3.8 mmHg ($p=0.011$) compared to naproxen. Furthermore, in contrast to naproxen, naproxcinod reduced the mean 24-hour SBP and diastolic blood pressure (DBP) from baseline at every dose comparison. Good safety and tolerability were shown by all naproxcinod doses. NicOx plans to provide further details of the results at a leading cardiology conference in 2009.

Naproxcinod is the first investigational drug in the new Cyclooxygenase-Inhibiting Nitric Oxide-Donator (CINOD) class of anti-inflammatory agents, which is nearing the end of phase 3 clinical development for the treatment of the signs and symptoms of osteoarthritis, with the submission of a New Drug Application (NDA) with the US Food and Drug Administration (FDA) projected for mid-2009. NicOx expects to have the results of a second large ABPM study in patients with hypertension and OA (112) before the end of 2008, in addition to the results of the remaining pivotal phase 3 trial in hip OA (303).

COX-2 inhibitors and traditional non-steroidal anti-inflammatory drugs (NSAIDs), such as naproxen and ibuprofen, are widely used as symptomatic treatments for OA. However, they can cause new episodes of high blood pressure and destabilize previously controlled hypertensive patients, which is a particular concern in the OA population where approximately 50% of patients are estimated to be hypertensive.

"These impressive results suggest that naproxcinod could represent a valuable treatment alternative for osteoarthritis patients," said Raymond Townsend, Professor of Medicine at the University of Pennsylvania, who advised NicOx on the design and analysis of the study. "The hypertensive side effects of COX-2 inhibitors and traditional NSAIDs are a serious medical issue and there is a clear need for a new drug with no detrimental effect on blood pressure. These ABPM data have been obtained in a relevant population of chronically treated osteoarthritis patients with many cardiovascular risk factors and clearly show a consistent beneficial effect on blood pressure for naproxcinod across the dose range, in contrast to naproxen. In addition, the use of the ABPM technique gives them considerable weight, as it is widely recognized as the gold standard method for assessing the blood pressure profile of new drugs."

The 111 study design and results

In the study, 118 patients were randomized on a 1:1 basis to receive naproxcinod or naproxen, with escalating doses every three weeks. The trial included three doses of naproxcinod (375 mg bid, 750 mg bid and a supra-therapeutic dose of 1125 mg bid), which were compared to naproxen (250, 500 and 750 mg bid). 24-hour blood pressure monitoring was conducted at baseline and at the end of each three-week dose escalation (i.e. at the end of week 3, 6 and 9), using an FDA validated, ABPM device.

The primary objective of the study was to characterize the 24-hour arterial blood pressure profile of the three doses of naproxcinod, as measured by ABPM after each dose, compared to naproxen. At all time points, naproxcinod showed a decrease in the mean 24-hour SBP and DBP from baseline in contrast to naproxen. In terms of the overall treatment effect, as an average over week 3, 6 and 9, naproxen raised SBP by 1.5 mmHg from baseline, while naproxcinod lowered it by 2.3 mmHg, resulting in a difference between the two treatments of 3.8 mmHg ($p=0.011$) in favor of naproxcinod.

Michele Garufi, Chairman and CEO of NicOx, commented: *"These excellent results are an important addition to the consistent data we are accumulating on naproxcinod's potentially non-detrimental blood pressure profile and its clear differentiation from naproxen. We are confident that naproxcinod's potential will be confirmed by the further clinical results expected in the coming months."*

The three doses of naproxcinod showed good general safety and tolerability. In the naproxcinod arm 32 patients (54.2%) experienced one or more adverse events, compared to 38 patients (64.4%) in the naproxen arm. There were no serious adverse events in the naproxcinod arm.

NicOx S.A.,

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Additional note on study design: The 111 study was a 12-week pharmacodynamic ABPM trial (with 9 weeks of active treatment), with a double-blind, parallel group design, in which 118 OA patients with controlled hypertension were enrolled at 30 clinical sites in the United States. Eligible patients were 40 years and older and had been suffering from osteoarthritis for at least three months, with at least one hip or knee involved. In addition to OA, all patients were diagnosed with controlled essential hypertension (i.e. SBP <140 mmHg and DBP <90 mmHg) and were treated with stable doses of up to two different classes of antihypertensive agents. Patients with uncontrolled hypertension were excluded.

NicOx (Bloomberg: COX:FP, Reuters: NCOX.PA) a product-driven biopharmaceutical company dedicated to the development and future commercialization of investigational drugs for unmet medical needs. NicOx is applying its proprietary nitric oxide-donating technology to develop an internal portfolio of New Chemical Entities (NCEs) in the therapeutic areas of inflammatory and cardio-metabolic disease.

Resources are focused on the development of naproxinod, a proprietary NCE and the first compound in the Cyclooxygenase-Inhibiting Nitric Oxide-Donating (CINOD) class of anti-inflammatory agents, which is in phase 3 clinical studies for the treatment of the signs and symptoms of osteoarthritis, with final phase 3 results anticipated in 2008.

Beyond naproxinod, NicOx has a pipeline containing multiple nitric oxide-donating NCEs, which are in development internally and with partners, including Pfizer Inc and Merck & Co., Inc., for the treatment of prevalent and underserved diseases, such as atherosclerosis, hypertension, widespread eye diseases and Chronic Obstructive Pulmonary Disease (COPD).

NicOx S.A. is headquartered in France and is listed on the Euronext Paris Stock Exchange (Compartment B: Mid Caps).



This press release contains certain forward-looking statements. Although the Company believes its expectations are based on reasonable assumptions, these forward-looking statements are subject to numerous risks and uncertainties, which could cause actual results to differ materially from those anticipated in the forward-looking statements.

For a discussion of risks and uncertainties which could cause actual results, financial condition, performance or achievements of NicOx S.A. to differ from those contained in the forward-looking statements, please refer to the Risk Factors ("Facteurs de Risque") section of the Document de Reference filed with the AMF, which is available on the AMF website (<http://www.amf-france.org>) or on NicOx S.A.'s website (<http://www.nicox.com>).

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